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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,989	09/17/2003	Shmuel A. Ben-Sasson	24348-502	4634

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EXAMINER	
TRAN, SUSAN T	
ART UNIT	**PAPER NUMBER**
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,989	BEN-SASSON ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *5-16,19-21,26-28,32,42-46 and 54-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,17,18,22-24,29-31,33-41,47-53 and 66-69* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II (claims 17 and 18) in the reply filed on 11/29/06 is acknowledged.

In the Remarks filed 11/29/06, at page 2, applicant states that: "Moreover, claims 2, 4, 11, 15-16, 22-25, 29-31, 42 and 45 read on the elected species." However, it is noted that claims 11, 15, 16, 42 and 45 belong to nonelected inventions (see page 2 of the Restriction Requirement dated 10/31/06). Accordingly, claims 5-16, 19-21, 26-28, 32, 42-46 and 54-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or specie, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/29/06.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 17, 18, 22-25, 29-31, 33-41 and 47-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 16, 17, 31-35, 39-48, 50, 51 and 55-61 of copending Application No. 11/489391 ('391). Although the conflicting claims are not identical, they are not patentably distinct from each other because application '391 claimed a composition for non-invasive translocation of at least one effector across a biological barrier, said composition comprising: (a) a therapeutically effective amount of said at least one effector; and (b) a counter ion to the at least one effector. Capsule is found in claim 4. At least one effector is a pharmaceutically active agent is found in claims 16 and 17. Counter ion is found in claims 31-35. Anionic molecule, surfactant, hydrophobic carrier, and protective agent are found in claims 39-48, 50, 51 and 55-61. Thus, the present claims are anticipated by the claims of the '391 application.

Claims 1-4, 17, 18, 22-25, 29-31, 33-41 and 47-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 12, 14, 15, 23-27, 38, 66-68, 70-73, 76 and 78 of copending Application No. 10/942300 ('300). Although the conflicting claims are not identical, they are not patentably distinct from each other because application '300 claimed a composition for transepithelial delivery of at least one effector, comprising a

therapeutically effective amount of said at least one effector; a counter ion to the at least one effector; and at least one pharmaceutically acceptable hydrophobic agent, wherein the at least one effector is capable of efficiently translocating across a biological barrier. Counter ion is found in claims 23-27. Surfactant in found in claims 66-68. Capsule is found in claim 78. Thus, the present claims are anticipated by the claims of the '391 application.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Claims 1, 3, 4, 29-31, 33-41 and 47-53 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 17-23, 26-30, 33, 34 and 40 of U.S. Patent No. 7,115,707 ('707). Although the conflicting claims are not identical, they are not patentably distinct from each other because patent '707 claimed a penetration composition for non-invasive translocation of at least one effector across a biological barrier, said composition comprising: (a) a therapeutically effective amount of said effector; and (b) a counter ion to the effector. Capsule is found in claim 3. Polyanionic molecule and surfactant are found in claims 17-20. Protective agent and non-ionic detergent are found in claims 26-30. Hydrophobic carrier such as tricaprine is found in claim 40. Thus, claims of the present invention are anticipated by the claims of the '707 patent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 17, 18, 22-24, 29, 30, 33-41, 47, 52, 53 and 66-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyurik US 2004/0176476, in view of Cooper et al. US 6,908,626.

Gyurik teaches a composition comprising a pharmaceutically active compound, or a mixture of two or more compounds capable of being delivered across a body membrane (paragraph 0014, lines 1-4). Pharmaceutically active compound includes insulin (paragraph 0015 lines 1-5). Gyurik further teaches the use of an enhancer capable of increasing the rate of passage of the pharmaceutically active compound through a membrane. Essentially any suitable solid or liquid enhancer or a mixture of such enhancers may be used in the practice of the present invention. Preferred enhancers are characterized by at least one of the following properties: membrane-compatibility; lipophilic nature; low level of irritability or no irritability to the target membrane; emolliency; and being a solid at room temperature when in neat form (paragraph 0025, lines 1-10). Membrane-compatible permeation enhancers are particularly preferred for use in the present invention. The term "membrane-compatible permeation enhancer" means a compound which increases the rate of delivery of the pharmaceutically active compound through the membrane without damage. Examples

of lipophilic membrane-compatible enhancers for use in the present invention include: fatty acids; fatty alcohols; alkyl esters, such as isopropyl myristate and myristyl myristate; and cycloaliphatic enhancers (paragraph 0026, lines 1-10). Gyurik also teaches that the pharmaceutical composition of the invention comprises an enzyme inhibitor which is capable of inhibiting breakdown and a suitable inhibitor may be selected form a group consisting leupetin, bestain and aprotinin (paragraph 0050, lines 1-19). The active compounds of the composition of may exist in either the continuous or the dispersed phase or in both phases depending upon whether the compounds are hydrophilic, lipophilic, or amphiphilic. In an example of a preferred embodiment of the present invention, the emulsion comprises oil droplets dispersed in a continuous aqueous phase with a lipophilic enhancer being contained in the oil droplets and a water-soluble pharmaceutically active compound dissolved in the continuous aqueous phase (paragraph 0038, lines 1-13). Gyurik also teaches that the pharmaceutical composition of the invention comprises insulin and benzalkonium (page 7 Example 1, part D and E).

Gyurik does not explicitly teach the claimed counter ion such as imidazolium derivatives.

Cooper teaches a composition comprising at least one poorly soluble active ingredient, at least one stabilizer, and one or more non-toxic physiologically acceptable carriers suitable for oral, rectal, or topical administration (abstract; and column 8, lines 35-48). Stabilizer includes an alkylimidazolium salt (column 13, lines 8-10). Thus, it would have been obvious to one of ordinary skill in the art to modify the composition of

Gyurik using alkylimidazolium salt as a surfactant or stabilizer in view of the teaching of Cooper to obtain the claimed invention, because Cooper teaches a stable dispersion of poorly soluble active agent in the present of one or more stabilizer (column 17, lines 40-45), because Gyurik teaches the desirability of obtaining a stable composition, and because Gyurik teaches the use of surfactant and/or stabilizer.

Claims 1-4, 17, 18, 22-24, 47-49, 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poli et al. US 5,654,000, in view of Cooper et al. US 6,908,626.

Poli teaches a composition for transmucosal administration comprising drug, stabilizer, and a thermosetting vehicle comprising pluronic polymer (column 3, lines 1 through column 4, lines 1-34). Drugs include cyclosporine and insulin (ID). The composition is in the form of soft gelatin capsule (ID).

Poli does not explicitly teach the claimed counter ion such as imidazolium derivatives.

Cooper teaches a composition comprising at least one poorly soluble active ingredient, at least one stabilizer, and one or more non-toxic physiologically acceptable carriers suitable for oral, rectal, or topical administration (abstract; and column 8, lines 35-48). Stabilizer includes an alkylimidazolium salt (column 13, lines 8-10). Thus, it would have been obvious to one of ordinary skill in the art to modify the composition of Poli using alkylimidazolium salt as a stabilizer in view of the teaching of Cooper to obtain the claimed invention, because Cooper teaches a stable dispersion of poorly

soluble active agent with the present of one or more stabilizer (column 17, lines 40-45), because Poli teaches the desirability of using a stabilizer.

Claims 1, 3, 4, 17, 18, 29-31, 35-39, 68 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poli et al., in view of Chen et al. US 6,267,985.

Poli is relied upon for the reason stated above. Poli does not teach the use of triglyceride.

Chen teaches a carrier system comprising triglyceride as an absorption enhancer for poorly soluble drugs (abstract; column 3, lines 1-62). The carrier system further comprises at least two surfactants including pluronic, poloxamer, and polyethylene glycol (tables 2-16). Thus, it would have been obvious to one of ordinary skill in the art to modify the carrier system of Poli using the carrier system in view of the teaching of Chen, because Chen teaches a carrier system that is thermodynamically stable, because Chen teaches a carrier system suitable for poorly soluble drugs such as cyclosporine, and because Poli teaches the desirability of obtaining a carrier system suitable for poorly soluble active agents.

Claims 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poli et al., in view of Chen et al. US 6,267,985 and Modi et al. US 5,653,987.

Poli and Chen are relied upon for the reasons stated above. The references do not teach the use of taurodeoxycholate.

Modi teaches a pharmaceutical composition for oral delivery comprising proteinic active agent, and an absorption enhancing compounds including taurodeoxycholate (abstract). Thus, it would have been obvious to one of ordinary skill in the art to include taurodeoxycholate in the carrier system to enhance absorption of the active agent, because Modi teaches a carrier system including the use of taurodeoxycholate suitable for active agent including insulin, and because Poli desired a carrier system suitable for transmucosal delivery of insulin.

Claims Allowable

Claim 25 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Pertinent Arts

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Hauer et al., and Gizurarson et al. are cited as of interest for the teachings of carrier compositions suitable for mucosal administration.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN TRAN
PRIMARY EXAMINER

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